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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte CHENG LI and MIR IMRAN

Appeal 2010-010447
Application 10/664,697
Technology Center 1600

Before DEMETRA J. MILLS, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, Administrative Patent Judges.

PRATS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to polypeptide compositions. The Examiner entered a rejection for obviousness.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

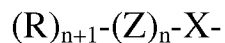
“Novel branched multiple arm peptides (or multiple antigenic peptides) (MAPs) and those MAPs which are covalently bonded to a substrate (S) are described as compositions of matter and as components of

implants in the present invention” (Spec. 15). The Specification discloses that the “covalently bound MAPs have at least one terminus (and optionally more than one terminus) attached to a substrate (S) and multiple arms which terminate in the same or different organic groups which have a variety of biological functions in vivo” (id.).

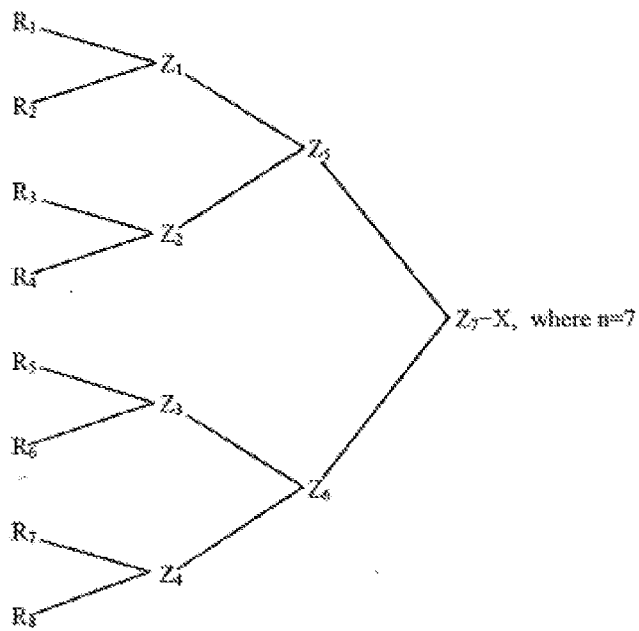
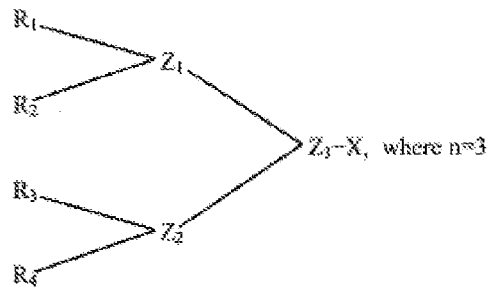
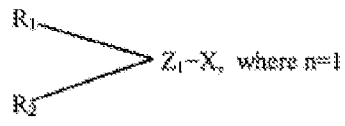
In vivo functions of Appellants’ disclosed MAPs “include but are not limited to increased cell adhesion, attachment, migration, proliferation, differentiation and the like, anti-inflammation properties, anti-thrombogenic properties, growth factor properties and the like” (id.). Thus, in certain embodiments, the MAPs’ terminal organic moiety has a cell adhesion molecule such as the “P-15” (SEQ ID NO: 1) peptide found in collagen (see id. at 11). MAP structures having terminal cell adhesion molecules are useful when affixed to implanted devices, such as grafts or stents (see id. at 2, 47-48).

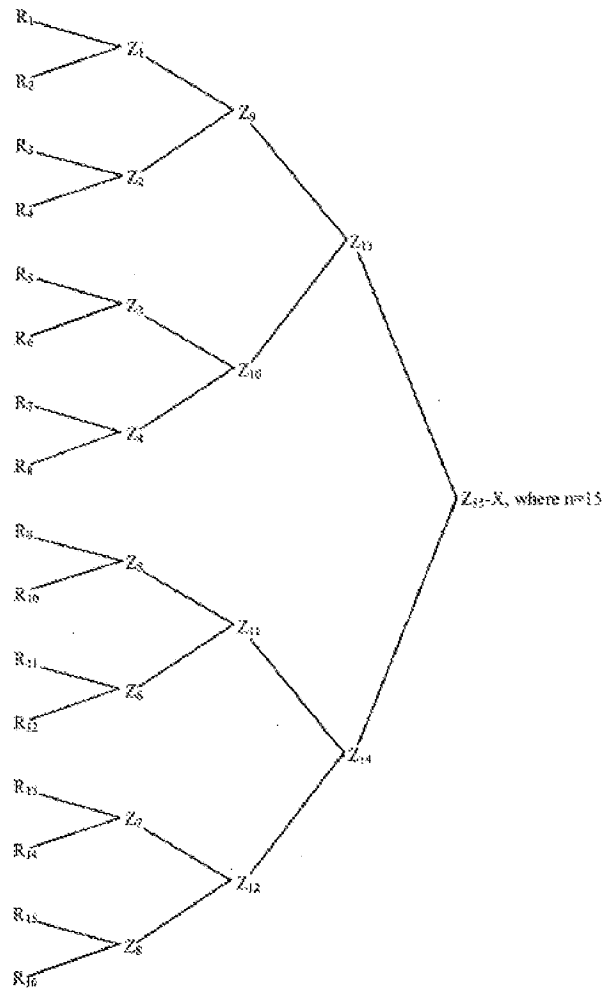
Claims 5, 6, 10-13, 18-22, 25, and 27-33 stand rejected and appealed (App. Br. 1). Claim 5, the only independent claim, is representative and reads as follows:

5. A composition of matter for the active structure MAP-S wherein MAP is an organic molecule which is covalently bound to a substrate S, wherein S is selected from the group consisting of metal, alloy, ceramic, natural polymer, synthetic polymer, bioabsorbable polymer, liquid polymer and combinations and blends thereof, and the organic structure MAP is selected from:



wherein n is selected from 1, 3, 7 or 15, producing the following structures:





each R contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations, with the proviso that, the MAP has active functional groups to covalently link the MAP structure to the surface of the substrate (S), located on group X, Z or R;

X is an active or protected linking group selected from the group consisting of amine, linked amino acids of 1 to 5 in length, (X1 to X5) which when present are the same or different, carboxylic acid, anhydride, hydroxyl, carbonyl succinimide (NHS) and siloxane;

each Z is independently selected from lysine or ornithine;

each R when present in the MAP structure comprises a total of up to about 100 amino acids, and wherein each R₁ to R₁₆ comprises GTPGPQGIAGQRGVV (SEQ ID NO: 1).

The following rejections are before us for review:

- (1) Claims 5, 6, 10-13, 18-22, 25, and 27-33, under 35 U.S.C. § 103(a) as obvious over Dang¹ and Tam² (Ans. 4-7); and
- (2) Claims 5, 10-13, 18-22 and 25, under 35 U.S.C. § 103(a) as obvious over Bhatnagar³ and Tam (Ans. 7-8).

OBVIOUSNESS – DANG AND TAM

The Examiner cites Dang as disclosing “stents and grafts and means of coating them with a peptide. The reference specifically discloses coating a substrate with the sequence GTPGPQGIAGQRGVV (called P-15) having the ability to provide enhanced endothelial cell growth in vitro” (Ans. 5).

The Examiner finds that Dang differs from the claims in that “the reference does not disclose the MAP structure” as the means by which the P-15 peptide is linked to the solid stent/graft substrate (id.).

To address that deficiency, the Examiner cites Tam as disclosing that “MAP structures can be applied in immunoassays, seradioagnosis [sic], epitope mapping, inhibitors, artificial proteins, and various biochemical studies and purification methods” (id. at 6). The Examiner notes the following teachings in Tam:

[A]s inhibitors, branched peptides with clustered positive charges can lead to stronger binding than their monomers by

¹ U.S. Patent App. Pub. No. 2003/0113478 A1 (filed December 12, 2001).

² James P. Tam, *Synthesis and Applications of Branched Peptides in Immunological Methods and Vaccines*, at pp. 455-500 of *PEPTIDES: SYNTHESIS, STRUCTURES, AND APPLICATIONS*, B. Gutte (ed.), Academic Press (1995).

³ WO 91/02537 A1 (published March 7, 1991).

allowing multiple points of contact (see page 476). Clustering could be achieved by adsorption on a surface or by coupling to a carrier or sepharose bead (see page 476). Observations of increased binding of branched peptides to cell surfaces, relative to the monomer, have been observed (see page 476).

Based on the references' teachings, the Examiner concludes that an ordinary artisan would have considered it obvious to incorporate the P-15 peptide "into a multimeric peptide structure (MAP) because branched peptides with clustered positive charges can lead to stronger binding than their monomers by allowing multiple points of contact and MAPs have increased binding to cell surfaces, relative to the monomer" (id.).

Appellants argue that neither Dang nor Tam, "alone or in combination, would have suggested each and every element of the claimed subject matter. The Examiner has failed to provide articulated reasoning based on a rational underpinning to support the legal conclusion of obviousness" (App. Br. 6 (citing MPEP 2143.01, paragraph IV; also citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007))). Furthermore, Appellants argue, "Tam et al. teaches away from any relevant modification of this document" (id.).

Specifically, Appellants urge that the MAP structures in the appealed claims function as "cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, or adhesive or adhesion barrier structures . . . [which] act as agonists to promote the function that the peptide GTPGPQGIAGQRGVV would normally have as presented in vivo" (id. at 6-7). In contrast to the agonist function of the claimed MAP peptides, Appellants argue, "Tam regards immunogenicity and antigenicity as

necessary for producing the branched peptides described therein and draws a distinction between these two criteria” (id. at 7).

Thus, Appellants reason, because Tam does not “indicate that it is necessary to retain the biological activity of the peptides or proteins used to make branched peptides,” Tam therefore “could not have possibly guided one of skill in the art to the claimed subject matter, which recites that the R portion of the MAP-S structure ‘contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations.’” (Id. at 7; see also Reply Br. 1-2).

Appellants further argue that Tam teaches away from the claimed invention (App. Br. 7). Specifically, Appellants argue, because Tam teaches that including a peptide in a MAP structure produces an inhibitor due to branched peptides with clustered positive charges (Tam at page 476), an ordinary artisan would have expected that “including GTPGPQGIAGQRGVV in a MAP structure would produce an inhibitor rather than the agonists recited by the present claims. Clearly, the applied art would not have guided one to the claimed subject matter” (id.).

While this is arguably a close case, we conclude that the Examiner has the better position.

In *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the Supreme Court reaffirmed that “when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result.” Id. at 416.

Thus, the Court reasoned:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

Id. at 421.

In the instant case claim 5 recites a composition of matter in which the cell adhesion peptide P-15 is covalently linked, by way of a branched MAP peptide, to a substrate made of metal, alloy, ceramic, natural polymer, synthetic polymer, bioabsorbable polymer, liquid polymer, and combinations and blends thereof.

Claim 5 also recites that, in addition to covalently linking the MAP structure to the substrate, the MAP structures must contain “any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations.”

Similar to claim 5, Dang discloses the suitability of attaching any of a number of different cell adhesion molecules, including P-15, to the surface of a biological implant such as a graft or stent, to render it more biocompatible (see Dang [0036], [0090], [0093]). While it is undisputed that Dang does not use claim 5’s branched peptide MAP structures to bind the P-15 to the substrate, as the Examiner points out, Tam discloses that MAP structures were known in the art to be useful for binding biologically active peptides to immobilized substrates, creating structures useful in affinity purifications, for example (see Tam 475 (Table VI)).

Tam also discloses that MAP structures were advantageous in immobilizing antigenic peptides:

In a dramatic example, a MAP shows a sensitivity increase of over 10^8 -fold when compared to a peptide antigen in an enzyme-linked immunosorbent assay (ELISA). The combined results indicate that the use of MAPs may be the method of choice to produce antigens for solid-phase immunoassays

(Id. at 475-76.)

We acknowledge, as Appellants argue, that Tam primarily focuses on the advantages of MAPs in potentiating the antigenicity of peptides, as opposed to immobilizing cell-binding ligands of the P-15 type. We also acknowledge Tam's disclosure that, by clustering together multiple copies of a weakly cell-binding peptide, MAP structures confer to the peptide the capacity to better bind to pathogenic cells and inhibit them (id. at 476).

We are not persuaded, however, that these teachings would have dissuaded an ordinary artisan from using Tam's MAP structures to bind Dang's P-15, and other additional cell adhesion molecules, to a substrate. Rather, in view of the variety of applications described by Tam in which the biological binding properties of peptides are maintained while being bound to solid substrates, including affinity purifications and ELISAs (see id. at 475-76), we find that an ordinary artisan would have recognized from Tam that MAP structures were useful for covalently linking biologically active peptides to solid substrates.

We therefore agree with the Examiner that an ordinary artisan, advised by Tam that MAP structures were suitable for covalently linking biologically active peptides to solid substrates, would have been prompted to

use MAPs to bind P-15, as well as other cell adhesion molecules described in Dang, to Dang's substrates.

It may be true that Tam discloses that highly branched MAP structures lead to increased clustering, resulting in cell-inhibiting molecules (id. at 476). We note, however, that Appellants' claim 5 encompasses MAP structures with only two branches. Moreover, Appellants have not clearly explained, and it is unclear why, an ordinary artisan would have viewed Tam as suggesting that clustering of a cell ingrowth and adhesion-promoting molecule such as P-15 would so significantly alter its activity as to render it a cell growth inhibitor.

In sum, for the reasons discussed, Appellants' arguments do not persuade us that the Examiner erred in finding that an ordinary artisan would have been prompted to use the claimed MAP structures to covalently link P-15, as well as other cell adhesion molecules described in Dang, to Dang's substrate. We therefore affirm the Examiner's obviousness rejection of claim 5 over Dang and Tam.

Because they were not argued separately, claims 6, 10-13, 18-22, 25, and 27-33 fall with claim 5. See 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS – BHATNAGAR AND TAM

The Examiner applies a similar rationale in rejecting claims 5, 10-13, 18-22 and 25 over Bhatnagar and Tam. Specifically, the Examiner cited Bhatnagar as disclosing that coating a substrate such as glass, plastic, organic polymers, gels, or silica, with P-15 promotes vertebral cell adhesion to the substrate (Ans. 7).

While the Examiner acknowledged that Bhatnagar did not use a MAP structure to bind the P-15 to the substrate to achieve the structure required by Appellants' claims, the Examiner nonetheless reasoned that an ordinary artisan would have been prompted by Tam to use MAPs to link P-15 to Bhatnagar's substrates (*id.* at 7-8).

Appellants reiterate essentially the same arguments made with respect to the rejection discussed above (see App. Br. 9-13; Reply Br. 3-4). We do not find these arguments persuasive of Examiner error.

As discussed above, given Tam's disclosure that MAPs were useful for binding biologically active peptides to solid substrates, allowing use of the immobilized peptides in affinity purifications and ELISAs (see Tam 475-76), we find that an ordinary artisan would have recognized from Tam that MAP structures would be useful for covalently linking other biologically active peptides, such as cell adhesion molecules, to solid substrates.

We therefore agree with the Examiner that an ordinary artisan, advised by Tam that MAP structures were suitable for covalently linking biologically active peptides to solid substrates, would have been prompted to use MAPs to bind Bhatnagar's P-15 to its substrates, thus meeting the structure required by Appellants' claim 5. In this regard, while we note claim 5's recitation that "each R contains any type and number of cell-binding ligands, anti-inflammatory structures, anti-thrombogenic structures, growth factor structures, adhesive or adhesion barrier structures, and their combinations," we also note that nothing in claim 5 excludes P-15 from being one of those moieties.

We also note again that the main focus of Tam was on the capacity of MAPs to generate highly antigenic species, and that Tam contained no

specific or explicit statement to the effect that MAPs were useful for linking cell adhesion molecules to solid substrates. However, given Tam's disclosure of the suitability of MAPs for linking biologically active peptides to solid substrates in applications such as affinity purifications and ELISAs (Tam 475-476), we are not persuaded that an ordinary artisan would have narrowly interpreted Tam as teaching that MAPs were only suitable for potentiating the antigenicity of peptides.

Thus, as the Supreme Court noted in *KSR*, in determining whether the prior art supplies a reason for practicing the claimed subject matter, the analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; see also *id.* at 421 ("A person of ordinary skill is . . . a person of ordinary creativity, not an automaton.").

In sum, Appellants' arguments do not persuade us that the Examiner erred in finding that an ordinary artisan would have been prompted to use the claimed MAP structures to covalently link Bhatnagar's P-15 to a solid substrate. We therefore affirm the Examiner's obviousness rejection of claim 5 over Bhatnagar and Tam.

As they were not argued separately, claims 10-13, 18-22 and 25, fall with claim 5. See 37 C.F.R. § 41.37(c)(1)(vii).

SUMMARY

- (1) Claims 5, 6, 10-13, 18-22, 25, and 27-33, under 35 U.S.C. § 103(a) as obvious over Dang and Tam (Ans. 4-7); and
- (2) Claims 5, 10-13, 18-22 and 25, under 35 U.S.C. § 103(a) as obvious over Bhatnagar and Tam (Ans. 7-8).

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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